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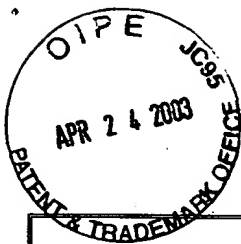
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09209/1653  
#16

PATENT  
ATTORNEY DOCKET NO. 50211/005002

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April 18, 2003

I hereby certify under 37 C.F.R. § 1.8(a) that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated above and is addressed to the Commissioner for Patents, Washington, D.C. 20231.

Julie A. Bowen

Printed name of person mailing correspondence

Julie A. Bowen

Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Judes Poirier

Art Unit: 1653

Serial No.: 09/342,993 ✓

Examiner: Karen C. Carlson

Filed: June 29, 1999

Customer No.: 21559

Title: APOLIPOPROTEIN E POLYMORPHISM AND TREATMENT OF ALZHEIMER'S DISEASE

Commissioner for Patents  
Washington, D.C. 20231

PETITION TO WITHDRAW NOTICE OF ABANDONMENT

Under 37 C.F.R. §§ 1.8(b) and 1.181, applicant hereby petitions to have the Notice of Abandonment that was mailed in connection with the above-captioned case on April 9, 2003 withdrawn. A copy of the Notice is enclosed. According to the Notice, the application was abandoned under 37 C.F.R. § 1.135 for applicant's failure to reply to a Office Action that was mailed on July 17, 2002. However, a reply was timely filed on December 16, 2002, including a Notice of Appeal and a Petition for Extension of Time.

The undersigned, applicant's attorney of record, first became aware of the abandonment on April 14, 2003, upon receipt of the Notice of Abandonment and submits

that this petition to withdraw the Notice is being promptly submitted as required by 37 C.F.R. § 1.8(b)(1).

The following documents are submitted under 37 C.F.R. § 1.8(b)(2) as proof that a reply was timely filed on December 16, 2002:

1. A copy of the reply, including an executed certificate of mailing signed by Tracey Simmons on December 16, 2002.
2. A copy of the Petition for Extension of Time, including an executed certificate of mailing signed by Tracey Simmons on December 16, 2002, which extended the period for replying to the Office Action for two months, to and including December 17, 2002;
3. A copy of the Notice of Appeal from the Examiner to the Board of Patent Appeals and Interferences under 37 C.F.R. § 1.191, including an executed certificate of mailing signed by Tracey Simmons on December 16, 2002;
4. A copy of a two checks dated December 16, 2002 and a copy of the postcard dated December 16, 2002 that were included with the reply and Petition for Extension.
5. A copy of two cancelled checks which cleared on December 27, 2002 and the postcard that was stamped as having been received by the PTO Mailroom on December 23, 2002.

Applicant submits that the reply was timely filed and requests that the Notice of Abandonment be withdrawn.

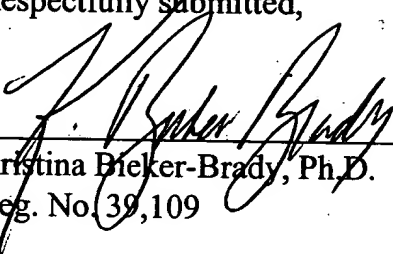
If there are any charges or any credits, please apply them to Deposit Account No.

03-2095.

Respectfully submitted,

Date:

April 17, 2003

  
\_\_\_\_\_  
Kristina Bieker-Brady, Ph.D.  
Reg. No. 39,109

Clark & Elbing LLP  
101 Federal Street  
Boston, MA 02110  
Telephone: 617-428-0200  
Facsimile: 617-428-7045





PATENT  
ATTORNEY DOCKET NO: 50211/005002

Certificate of Mailing: Date of Deposit: December 14, 2002

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Tracey Simmons  
Printed name of person mailing correspondence

Tracey Simmons  
Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Judes Poirier Art Unit: 1653  
Serial No.: 09/342,993 Examiner: Karen C. Carlson  
Filed: June 29, 1999 Customer No.: 21559  
Title: APOLIPOPROTEIN E POLYMORPHISM AND TREATMENT OF  
ALZHEIMER'S DISEASE  
BOX AF  
Commissioner for Patents  
Washington, DC 20231

REPLY TO EXAMINER'S ACTION

In reply to the Examiner's Action mailed July 17, 2002, Applicant makes the following amendments and remarks.

AMENDMENT

Kindly amend the claims as follows.

In the Claims:

1. (Twice Amended) A method for the identification of human subjects having Alzheimer's disease responsive to treatment with a cholinomimetic drug, said method comprising determining the presence of *apoE4* gene alleles in said subject, wherein the absence of an *apoE4* gene allele in a biological sample of said subject identifies said subject

as a subject whose Alzheimer's disease-related cognitive impairment is responsive to treatment with a cholinomimetic drug.

4. (Twice Amended) A method for genotyping a patient sample with respect to apoE4 allele in a clinical trial of a drug for the treatment of cognitive impairments, said method comprising:

(a) identifying a patient already diagnosed with said cognitive impairments, or as being predisposed to acquire or to be at risk for said cognitive impairments; and

(b) determining the presence of *apoE4* gene alleles in said patient, wherein the genotype of said patient sample with respect to apoE4 allele in a clinical trial of said drug allows the effects of said drug to be compared according to apoE4 genotype.

5. (Twice Amended) A method for genotyping a patient sample with respect to apoE4 allele in a clinical trial of a drug for the treatment of Alzheimer's disease, said method comprising:

(a) identifying a patient already diagnosed with said Alzheimer's disease or as being predisposed to acquire or to be at risk for said disease; and

(b) determining the presence of *apoE4* gene alleles in said patient, wherein the genotype of said patient sample with respect to apoE4 allele in said clinical trial of a drug for the treatment of said Alzheimer's disease allows the effects of said drug to be compared according to apoE4 genotype.

## REMARKS

Claims 1-5 and 8 are under examination in the present case. Each of these claims is rejected under 35 U.S.C. § 112, second paragraph. The rejections are addressed below.

### Support for the amendments

Support for the amendments is found throughout the specification; for example, support for the amendment of claim 1, which now recites “Alzheimer’s disease-related cognitive impairment” is found at page 26, lines 3-26; and at Figure 8. Support for the amendment of claims 4 and 5, which now recite “genotype of said patient sample with respect to apoE4 allele ” is found at page 6, lines 12-18; at page 6, lines 32-34; at page 10, lines 10-19; and at page 26, lines 27-31.

### Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-5 and 8 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite.

The Examiner rejects independent claim 1, and dependent claims 2 and 3, as indefinite for reciting “beneficial effects.” In accordance with the Examiner’s suggestion, the amended claims now recite “Alzheimer’s disease-related cognitive impairment is responsive to treatment.”

The Examiner rejects claims 4 and 5 as indefinite. The Examiner asserts that the claims are indefinite in specifying the patient’s group placement and treatment. The claims have been amended to clarify that the genotype of the patient sample (i.e., the patient’s apoE4 allele) is used to compare the effects of the drug on patients having different apoE4 genotypes. As shown in Figure 8, apoE4 genotype is useful in comparing the effects of a drug in a clinical trial. The indefiniteness rejections may be withdrawn.

Rejection under doctrine of obviousness-type double patenting

Claims 1-5 and 8 are rejected as being unpatentable over claims 1-4 of U.S. Patent No. 5,935,781 ('781 patent). To overcome this rejection, Applicant will submit a terminal disclaimer in compliance with 37 C.F.R. 1.321(c) once notice of otherwise allowable subject matter is received.

CONCLUSION

Applicant submits that this case is in condition for allowance, and such action is respectfully requested. If the Office does not concur, a telephonic interview with the undersigned is hereby requested.

A marked-up version indicating the amendments to the claims, and a clean version of all pending claims is enclosed.

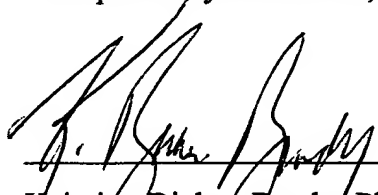
Enclosed is a petition to extend the period for replying for two months, to and including December 17, 2002. Also enclosed is a Notice of Appeal to the Board of Patent Appeals and Interferences.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date:

December 16, 2002

  
\_\_\_\_\_  
Kristina Bieker-Brady, Ph.D.  
Reg. No. 39,109

Clark & Elbing LLP  
101 Federal Street  
Boston, MA 02110  
Telephone: 617-428-0200  
Facsimile: 617-428-7045



21559

PATENT TRADEMARK OFFICE



Version of Claims Showing Changes Made

1. (Twice Amended) A method for the identification of human subjects [to be responsive to a cholinomimetic drug, said subjects,] having Alzheimer's disease responsive to treatment with a cholinomimetic drug, said method comprising determining the presence of *apoE4* gene alleles in said subject, wherein the absence of an *apoE4* gene allele in a biological sample of said subject [indicates a predisposition to receive beneficial effects from] identifies said subject as a subject whose Alzheimer's disease-related cognitive impairment is responsive to treatment with a cholinomimetic drug.

4. (Twice Amended) A method for genotyping [identifying] a patient sample with respect to *apoE4* allele in a clinical trial of a drug for the treatment of cognitive impairments, said method comprising:

(a) identifying a patient already diagnosed with said cognitive impairments, or as being predisposed to acquire or to be at risk for said cognitive impairments; and

(b) determining the presence of *apoE4* gene alleles in said patient, wherein [absence of an *apoE4* allele places the patient into a group that either receives or does not receive] the genotype of said patient sample with respect to *apoE4* allele [said drug for said] in a clinical trial of said drug allows the effects of said drug to be compared according to *apoE4* genotype.

5. (Twice Amended) A method for genotyping [identifying] a patient sample with respect to *apoE4* allele in a clinical trial of a drug for the treatment of Alzheimer's disease, said method comprising:

(a) identifying a patient already diagnosed with said Alzheimer's disease or as being predisposed to acquire or to be at risk for said disease; and

(b) determining the presence of *apoE4* gene alleles in said patient, wherein the genotype of said patient sample with respect to *apoE4* allele [an absence of an *apoE4* allele places the patient into a subgroup] in said clinical trial of a drug for the treatment of said

Alzheimer's disease allows the effects of said drug to be compared according to apoE4 genotype.

### Claims Pending After Entry of Amendment

1. A method for the identification of human subjects having Alzheimer's disease responsive to treatment with a cholinomimetic drug, said method comprising determining the presence of *apoE4* gene alleles in said subject, wherein the absence of an *apoE4* gene allele in a biological sample of said subject identifies said subject as a subject whose Alzheimer's disease-related cognitive impairment is responsive to treatment with a cholinomimetic drug.

2. The method of claim 1, wherein said method further comprises administering to said subject having an absence of *apoE4* allele a therapeutically effective amount of a cholinomimetic drug.

3. The method of claim 2, wherein administration of the cholinomimetic drug improves cognitive performance.

4. A method for genotyping a patient sample with respect to *apoE4* allele in a clinical trial of a drug for the treatment of cognitive impairments, said method comprising:

(a) identifying a patient already diagnosed with said cognitive impairments, or as being predisposed to acquire or to be at risk for said cognitive impairments; and

(b) determining the presence of *apoE4* gene alleles in said patient, wherein the genotype of said patient sample with respect to *apoE4* allele in a clinical trial of said drug allows the effects of said drug to be compared according to *apoE4* genotype.

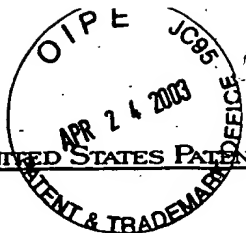
5. A method for genotyping a patient sample with respect to *apoE4* allele in a clinical trial of a drug for the treatment of Alzheimer's disease, said method comprising:

(a) identifying a patient already diagnosed with said Alzheimer's disease or as being predisposed to acquire or to be at risk for said disease; and

(b) determining the presence of *apoE4* gene alleles in said patient, wherein the genotype of said patient sample with respect to *apoE4* allele in said clinical trial of a drug for

the treatment of said Alzheimer's disease allows the effects of said drug to be compared according to apoE4 genotype.

8. The method of claims 1, 2, 3, 4, or 5, wherein said drug is tacrine.



## UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/342,993

06/29/1999

JUDES POIRIER

009237005002

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04/09/2003

CLARK & ELBING LLP  
101 FEDERAL STREET  
BOSTON, MA 02110

50211-005002

EXAMINER

CARLSON, KAREN C

ART UNIT

PAPER NUMBER

1653

DATE MAILED: 04/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

RECEIVED

APR 24 2003

CLARK &amp; ELBING

Petition to

ACTION DUE Withdrawal abandonment

DUE DATE \_\_\_\_\_

ESP 6-9-03INITIALS J.M.ACTION DUE Petition to Revoke

DUE DATE \_\_\_\_\_

ESP 4-9-04INITIALS J.M. JMB

PATENT  
ATTORNEY DOCKET NO. 50211/005002

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<u>Tracey Simmons</u>	<u>Tracey Simmons</u>
Printed name of person mailing correspondence	Signature of person mailing correspondence

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Judes Poirier	Art Unit:	1653
Serial No.:	09/342,993	Examiner:	Karen C. Carlson
Filed:	June 29, 1999	Customer No.:	21559
Title:	APOLIPOPROTEIN E POLYMORPHISM AND TREATMENT OF ALZHEIMER'S DISEASE		

BOX AF  
Commissioner for Patents  
Washington, D.C. 20231

NOTICE OF APPEAL FROM THE EXAMINER TO THE  
BOARD OF PATENT APPEALS AND INTERFERENCES UNDER 37 C.F.R. §1.191

Applicant respectfully appeals to the Board of Patent Appeals and Interferences from the decision dated July 17, 2002 of the Examiner finally rejecting claims 1-5 and 8.

Enclosed pursuant to 37 C.F.R. § 1.136 is a petition to extend the time to respond to the final rejection for two months, to and including December 17, 2002.

Also enclosed is a check in the amount of \$160.00 for the fee required by 37 C.F.R. § 1.17(b) for this Notice of Appeal. If there are any charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: December 16, 2002Kristina Bieker-Brady  
Kristina Bieker-Brady, Ph.D.  
Reg. No. 39,109

Clark 12/24/2002 00000053 1 2401 \$160.00 12/23/2002

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Boston, MA 02110

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21559

PATENT TRADEMARK OFFICE

PATENT  
ATTORNEY DOCKET NO. 50211/005002Certificate of Mailing: Date of Deposit: December 16, 2002

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Tracey Simmons

Printed name of person mailing correspondence

Tracey Simmons

Signature of person mailing correspondence

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Judes Poirier

Art Unit: 1653

Serial No.: 09/342,993

Examiner: Karen C. Carlson

Filed: June 29, 1999

Customer No.: 21559

Title: APOLIPOPROTEIN E POLYMORPHISM AND TREATMENT OF ALZHEIMER'S DISEASE

BOX AF

Commissioner for Patents

Washington, D.C. 20231

PETITION FOR EXTENSION OF TIME

Pursuant to 37 C.F.R. § 1.136, Applicant hereby petitions that the period for replying to the Examiner's Action, mailed July 17, 2002, be extended for two months to and including December 17, 2002.

Enclosed is a check for \$200.00 for the required fee under 37 C.F.R. § 1.17(a). If there are any other charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: December 16, 2002Kristina Bleker-Brady  
Kristina Bleker-Brady, Ph.D.  
Reg. No. 39,109

Clark &amp; Elbing LLP

12/24/2002

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\$200.00 12/23/2002

Telephone: 617-428-0200

Facsimile: 617-428-7045



21559

PATENT TRADEMARK OFFICE



# **Notice of Abandonment**

Applicant(s)	Applicant(s)
09/342,993	POIRIER, JUDES
Examiner	Art Unit
Karen Cochrane Carlson, Ph.D.	1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

This application is abandoned in view of:

1. ☒ Applicant's failure to timely file a proper reply to the Office letter mailed on 17 July 2002.
  - (a) ☐ A reply was received on \_\_\_\_\_ (with a Certificate of Mailing or Transmission dated \_\_\_\_\_), which is after the expiration of the period for reply (including a total extension of time of \_\_\_\_\_ month(s)) which expired on \_\_\_\_\_.
  - (b) ☐ A proposed reply was received on \_\_\_\_\_, but it does not constitute a proper reply under 37 CFR 1.113 (a) to the final rejection.  
(A proper reply under 37 CFR 1.113 to a final rejection consists only of: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114).
  - (c) ☐ A reply was received on \_\_\_\_\_ but it does not constitute a proper reply, or a bona fide attempt at a proper reply, to the non-final rejection. See 37 CFR 1.85(a) and 1.111. (See explanation in box 7 below).
  - (d) ☒ No reply has been received.
2. ☐ Applicant's failure to timely pay the required issue fee and publication fee, if applicable, within the statutory period of three months from the mailing date of the Notice of Allowance (PTOL-85).
  - (a) ☐ The issue fee and publication fee, if applicable, was received on \_\_\_\_\_ (with a Certificate of Mailing or Transmission dated \_\_\_\_\_), which is after the expiration of the statutory period for payment of the issue fee (and publication fee) set in the Notice of Allowance (PTOL-85).
  - (b) ☐ The submitted fee of \$\_\_\_\_\_ is insufficient. A balance of \$\_\_\_\_\_ is due.  
The issue fee required by 37 CFR 1.18 is \$\_\_\_\_\_. The publication fee, if required by 37 CFR 1.18(d), is \$\_\_\_\_\_.
  - (c) ☐ The issue fee and publication fee, if applicable, has not been received.
3. ☐ Applicant's failure to timely file corrected drawings as required by, and within the three-month period set in, the Notice of Allowability (PTO-37).
  - (a) ☐ Proposed corrected drawings were received on \_\_\_\_\_ (with a Certificate of Mailing or Transmission dated \_\_\_\_\_), which is after the expiration of the period for reply.
  - (b) ☐ No corrected drawings have been received.
4. ☐ The letter of express abandonment which is signed by the attorney or agent of record, the assignee of the entire interest, or all of the applicants.
5. ☐ The letter of express abandonment which is signed by an attorney or agent (acting in a representative capacity under 37 CFR 1.34(a)) upon the filing of a continuing application.
6. ☐ The decision by the Board of Patent Appeals and Interference rendered on \_\_\_\_\_ and because the period for seeking court review of the decision has expired and there are no allowed claims.
7. ☒ The reason(s) below:

  
KAREN COCHRANE CARLSON, PH.D.  
PRIMARY EXAMINER

Petitions to revive under 37 CFR 1.137(a) or (b), or requests to withdraw the holding of abandonment under 37 CFR 1.181, should be promptly filed to minimize any negative effects on patent term.





**\*\*PROSECUTION\*\***

PATENT

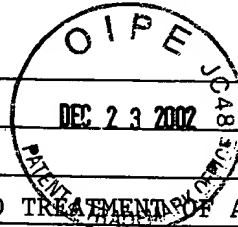
ATTORNEY DOCKET NUMBER: 50211/005002

The U.S. PTO date stamp sets forth the date of receipt of:

Applicant/Patentee: Judes Poirier

Serial/Patent Number: 09/342,993

Filed/Issued: June 29, 1999



Title: APOLIPOPROTEIN E POLYMORPHISM AND TREATMENT OF ALZHEIMER'S DISEASE

<input type="checkbox"/> Transmittal Letter	Pages: _____	<input type="checkbox"/> Declaration & POA	Pages: _____
<input type="checkbox"/> Notice to File Missing Parts	Pages: _____	<input type="checkbox"/> Assignment & Cover Sheet	Pages: _____
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<input checked="" type="checkbox"/> Petition for Extension	Pages: <u>1</u>	<input type="checkbox"/> IDS	Pages: _____
<input checked="" type="checkbox"/> Notice of Appeal	Pages: <u>1</u>	<input type="checkbox"/> Form PTO-1449	Pages: _____
<input type="checkbox"/> Appeal Brief	Pages: _____	<input type="checkbox"/> Cited References	Number: _____
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Atty/Secy: KBB/MHE/ Client/Matter Name: Variagenics/APOE Date: 12-16-02

The U.S. PTO date stamp sets forth the date of receipt of:

Applicant/Patentee: Judes Poirier

Serial/Patent Number: 09/342,993

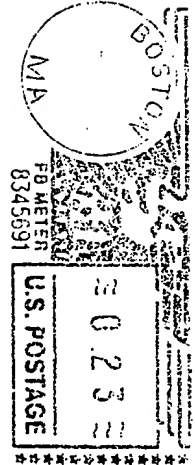
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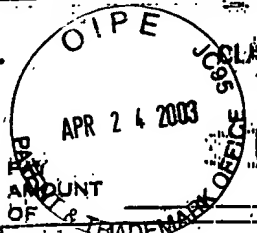
Title: APOLIPOPROTEIN E POLYMORPHISM AND TREATMENT OF ALZHEIMER'S DISEASE

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<input type="checkbox"/> Notice to File Missing Parts	Pages: _____	<input type="checkbox"/> Assignment & Cover Sheet	Pages: _____
<input type="checkbox"/> Reply to Missing Parts	Pages: <u>8</u>	<input type="checkbox"/> Change of Address	Pages: _____
<input checked="" type="checkbox"/> Reply to Office Action	Pages: <u>1</u>	<input type="checkbox"/> Preliminary Amendment	Pages: _____
<input checked="" type="checkbox"/> Petition for Extension	Pages: <u>1</u>	<input type="checkbox"/> IDS	Pages: _____
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Clark & Elbing LLP  
101 Federal Street  
Boston, MA 02110





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101 FEDERAL STREET  
BOSTON, MA 02110

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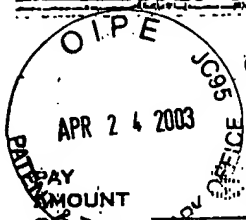
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12-24-2002  
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CLARK & ELBING LLP  
101 FEDERAL STREET  
BOSTON, MA 02110

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26-10-441

12109

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*[Signature]*



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U.S. TREASURY

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